**Application No.:** 10/664,697 **Office Action Dated:** July 27, 2006

This listing of claims will replace all prior versions, and listings, of claims in the application.

## **Listing of Claims:**

Claims 1-2 cancelled.

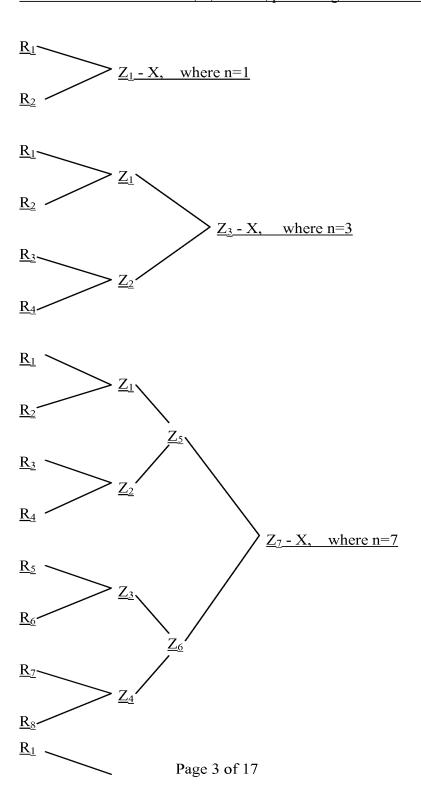
3. (Currently amended) The composition of matter of Claim  $\underline{5}$  [[2]] wherein  $R_1$  to  $R_{16}$  when present are each independently selected from the group consisting of total of up to about  $\underline{100}$  [[1500]] amino acids, anti-inflammatory agents, anti-thrombogenic agents and combinations thereof.

- 4. (Currently amended) The composition of matter of Claim <u>5</u> [[2]] wherein S is selected from the group consisting of hydroxyapatite, stainless steel, cobalt-chromium, molybdenum alloy, titanium, titanium alloy, polypropylene, polyethylene, polystyrene, polyether, polyamide/polyethylene copolymer, polychloroprene, polyester, polyvinyl chloride, polyolefin, polyphenolic, polyhydroxyacid, ABS epoxy, polytetrafluoroethylene, expanded polytetrafluoroethylene,
- polytetrafluoroethylene/polyethylene copolymer, fluorinated ethylene propylene, polyvinylidene, hexafluroropropylene, polyurethane, polysiloxane, polyisoprene, silicone, styrene butadiene, natural rubber, latex rubber, polyethyleneterephthalate, polycarbonate, polyamide, polyaramid, polyaryl ether ketone, polyacetal, polyphenylene oxide, polysulfone, polyethersulfone, regenerated cellulose, polyamino acids, polyarylsulfone, polyphenylene sulfide (PBT) poly(glycolide), HEMA and combinations thereof.
- 5. (Currently amended) A composition of matter for the active structure MAP-S wherein MAP is an organic molecule which is covalently bound to a substrate S, wherein S selected from the group consisting of metal, alloy, ceramic, natural polymer, synthetic polymer, bioabsorbable polymer, liquid polymer and combinations and blends thereof, and the organic structure MAP is selected from:

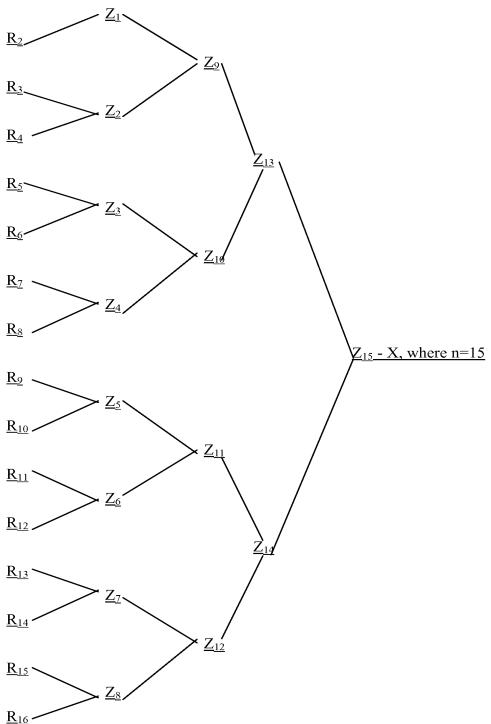
 $(R)_{n+1}$ - $(Z)_n$ -X-

**DOCKET NO.:** CUBE-0002 **Application No.:** 10/664,697 **Office Action Dated:** July 27, 2006

where n is selected from 1, 3, 7 or 15, producing the following structures:



**DOCKET NO.:** CUBE-0002 **Application No.:** 10/664,697 Office Action Dated: July 27, 2006



R and Z in each MAP structure are the same or a different moiety, each R contains any type and number of cell-binding ligands, anti-inflammatory structures, antithrombogenic, growth factor structures, adhesive or adhesion barrier structures, and their Page 4 of 17

**Application No.:** 10/664,697 **Office Action Dated:** July 27, 2006

combinations, with the proviso that, the MAP has active functional groups to covalently link the MAP structure to the surface of the substrate (S), located on group X, Z or R;

X is active or protected linking group selected from the group consisting of amine, linked amino acids of 1 to 5 in length, (X1 to X5) which when present are the same or different, carboxylic acid, anhydride, hydroxyl, carbonyl succinimide (NHS) and siloxane;

Z is independently selected from the group consisting of lysine, polylysine, ornithine or any trifunctional organic structure;

each Z when present in the MAP structure comprises a total of up to about 500 amino acids;

each R when present in the MAP structure comprise a total of up to about 200 amino acids, and The composition of matter of Claim 2 wherein R<sub>1</sub> to R<sub>16</sub> when present are independently selected from the group consisting of

GTPGPQGIAGQRGVV (SEQ ID NO: 1); RGD (SEQ ID NO: 2); REDV (SEQ ID NO: 3); WQPPRARI (SEQ ID NO: 4); YIGSR (SEQ ID NO: 5); SIKVAV (SEQ ID NO: 6); RYVVLPRPVCFEKGMNYTVR (SEQ ID NO: 7); GEFYFDLRLKGDK (SEQ ID NO: 8); GAG (SEQ ID NO: 9); QGIAGQ (SEQ ID NO: 10); KNEED (SEQ ID NO: 11); PDSGR (SEQ ID NO: 12); anti-inflammatory agents; antithrombogenic agents; growth factor agents; and adhesive or adhesion barrier agents.

6. (Original) The composition of matter of Claim 5 wherein S is selected from the group consisting of hydroxylapatite, stainless steel, cobalt-chromium, molybdenum alloy, titanium, Page 5 of 17

**Application No.:** 10/664,697 **Office Action Dated:** July 27, 2006

titan alloy, polypropylene, polyethylene, polystyrene, polyether, polyamide/polyethylene copolymer, polychloroprene, polyester, polyvinyl chloride, polyolefin, polyphenolic, polyhydroxyacid, ABS epoxy, polytetrafluoroethylene, expanded polytetrafluoroethylene, polytetrafluoroethylene/polyethylene copolymer, fluorinated ethylene propylene, polyvinylidene, hexafluroropropylene, polyurethane, polysiloxane, polyisoprene, silicone, styrene butadiene, natural rubber, latex rubber, polyethyleneterephthalate, polycarbonate, polyamide, polyaramid, polyaryl ether ketone, polyacetal, polyphenylene oxide, polysulfone, polyethersulfone, regenerated cellulose, polyamino acids, polyarylsulfone, polyphenylene sulfide, polybutyl-tere-phthalate (PBT) poly(glycolide), HEMA and combinations thereof.

- 7. (Currently amended) The composition of matter of Claim  $\underline{5}$  [[2]] wherein  $X_1$  and  $X_2$  when present and  $X_1$  or  $X_2$  and combinations thereof are each independently selected from the group consisting of lysine, polylysine, ornithine and alanine.
- 8. (Currently amended) The composition of matter of Claim  $\underline{5}$  [[2]] wherein  $Z_1$  to  $Z_{15}$  when presented is independently selected from the group consisting of lysine, ornithine and polylysine.
- 9. (Original) The composition of matter of Claim 7 wherein S is selected from the group consisting of hydroxylapatite, stainless steel, cobalt-chromium, molybdenum alloy, titanium, titan alloy, polypropylene, polyethylene, polystyrene, polyether, polyamide/polyethylene copolymer, polychloroprene, polyester, polyvinyl chloride, polyolefin, polyphenolic, polyhydroxyacid, ABS epoxy, polytetrafluoroethylene, expanded polytetrafluoroethylene, polytetrafluoroethylene/polyethylene copolymer, fluorinated ethylene propylene, polyvinylidene, hexafluroropropylene, polyurethane, polysiloxane, polyisoprene, silicone, styrene butadiene, natural rubber, latex rubber, polyethyleneterephthalate, polycarbonate, polyamide, polyaramid, polyaryl ether ketone, polyacetal, polyphenylene oxide, polysulfone, polyethersulfone, regenerated cellulose, polyamino acids, polyarylsulfone, polyphenylene sulfide (PBT) poly(glycolide), HEMA and combinations thereof.

Application No.: 10/664,697

Office Action Dated: July 27, 2006

10. (Currently amended) The composition of matter of Claim  $\underline{5}$  [[2]] wherein  $Z_1$  to  $Z_{15}$  is

lysine.

11. (Currently amended) The composition of matter of Claim 5 [[2]] wherein MAP is

MAP4 and R<sub>1</sub> to R<sub>4</sub> are each independently selected of from linear peptides having about 50

amino acids or less.

12. (Currently amended) The composition of matter of Claim 5 [[2]] wherein MAP is

MAP 8 and R<sub>1</sub> to R<sub>8</sub> are each independently selected from linear peptides having 50 amino

acids or less.

13. (Currently amended) The composition of matter of Claim 5 [[2]] wherein MAP is

MAP16 and R<sub>1</sub> to R<sub>16</sub> are each independently selected from linear peptides having about 50

amino acids or less.

14. (Currently amended) The composition of Claim  $\underline{5}$  [[2]] wherein  $R_1$  to  $R_{16}$  are each an

anti-inflammatory agent which is independently selected from aspirin, ibuprofen, naproxen,

or COX-2; or combinations thereof.

15. (Currently amended) The composition of matter of Claim  $\underline{5}$  [[2]] wherein R<sub>1</sub> to R<sub>16</sub>

when present are each anti-thrombogenic agents independently selected the group consisting

of from heparin, coumarin, hirudin, hirudin analogs and combinations thereof.

16. (Currently amended) The composition of matter of Claim  $\underline{5}$  [[2]] wherein R<sub>1</sub> to R<sub>16</sub>

when present are selected from growth factors.

17. (Currently amended) The composition of matter of Claim  $\underline{5}$  [[2]] wherein R<sub>1</sub> to R<sub>16</sub>

when present are selected from adhesion barrier agents.

18. (Currently amended) The composition of matter of Claim 5 [[2]] wherein

Page 7 of 17

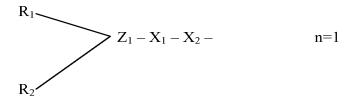
**Application No.:** 10/664,697 **Office Action Dated:** July 27, 2006

S is selected from the group consisting of polytetrafluoroethylene (PTFE) and hydroxylapatite;

 $X_1$  and  $X_2$  are selected from the group consisting of carboxyl and amino acid;  $Z_1$  to  $Z_{15}$  are lysine; and

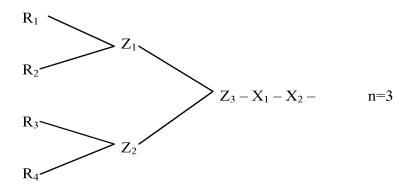
 $R_1 \ to \ R_{16} \ when \ present \ are selected \ from \ the \ group \ consisting \ of \ -Gly-Thr-Pro-Gly-Pro-Gly-Gly-Val-Val \ and \ RGD.$ 

19. (Currently amended) The composition of matter of Claim <u>5</u> [[2]] wherein: MAP is MAP2 of the structure:



Z is lysine and R<sub>1</sub> and R<sub>2</sub> are each -Gly-Thr-Pro-Gly-Pro-Gln-Gly-Gln-Arg-Gly-Val-Val or RGD;

MAP is MAP4 of the structure:

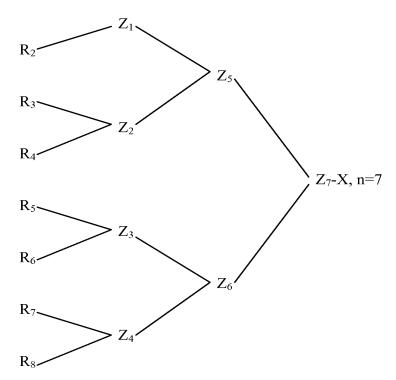


 $Z_1$ ,  $Z_2$  and  $Z_3$  are lysine and  $R^1$ ,  $R^2$ ,  $R^3$  and  $R^4$  are each -Gly-Thr-Pro-Gly-Pro-Gln-Gly-Gln-Arg-Gly-Val-Val or RGD; or

MAP is MAP8 of the structure:



**DOCKET NO.:** CUBE-0002 **Application No.:** 10/664,697 **Office Action Dated:** July 27, 2006



 $Z_1$  to  $Z_7$  are lysine and  $R_1$  to  $R_8$  are each selected from -Gly-Thr-Pro-Gly-Pro-Gln-Gly-Gln-Arg-Gly-Val-Val or RGD; and X is -X<sub>1</sub>- or -X<sub>1</sub>-X<sub>2</sub>- selected from lysine, ornithine or alanine.

- 20. (Currently amended) A pharmaceutical composition which comprises: a pharmaceutically acceptable amount of MAP of Claim <u>5</u> [[2]] in combination with a pharmaceutically acceptable carrier.
- 21. (Currently amended) A pharmaceutical composition which comprises a pharmaceutically acceptable amount of MAP2, MAP 4 or MAP 8 of Claim <u>5</u> [[2]] with a pharmaceutically acceptable carrier.
- 22. (Currently amended) An implant comprising: a matrix formed of a multiple arm peptide-substrate (MAP-S) formed of a biomaterials coated substrate S and a multiple MAP peptide of Claim 5 [[2]] combined by covalent bonding to the substrate, wherein the MAP peptide has terminal ligands which have enhanced properties for cell adhesion, migration, cell Page 9 of 17

**Application No.:** 10/664,697 **Office Action Dated:** July 27, 2006

differentiation, cell proliferation, anti-inflammation, anti-thrombogenesis, cell growth, adhesion barrier and combinations thereof.

23. (Currently amended) An implant comprising: a matrix formed of a multiple arm peptide-substrate (MAP-S) formed of a biomaterials coated substrate S and a multiple MAP peptide carried by covalent bonding to the substrate, wherein the MAP peptide has terminal ligands which have enhanced properties for cell adhesion, migration, differentiation, proliferation, anti-inflammation, anti-thrombogenesis, cell growth, adhesion barrier and combinations thereof,

wherein MAP-S has the MAP structure of Claim 5 [[2]].

24. (Original) An implant comprising: a matrix formed of a multiple arm peptide-substrate (MAP-S) formed of a biomaterials coated substrate S and a multiple MAP peptide carried by covalent bonding to the substrate, wherein the MAP peptide has terminal ligands which have enhanced properties for cell adhesion, migration, differentiation, proliferation, anti-inflammation, anti-thrombogenesis, cell growth, adhesion barrier and combinations thereof,

wherein MAP-S has the MAP structure of Claim 7.

- 25. (Original) The implant of Claim 22 wherein the peptide MAP has a peptide sequence selected from the group consisting of MAP ID NO: 13 MAP ID NO: 48 inclusive.
- 26. (Original) The implant of Claim 25 wherein the substrate is selected from polymer materials selected from hydrocarbons including polypropylene, polyethylene, polystyrene, polyether, polyamide/polyethylene copolymer, polychloroprene, polyester, polyvinyl chloride, polyolefin, polyphenolic, polyhydroxyacid, ABS epoxy, and corresponding copolymers and blends;

fluorocarbons-including polytetrafluoroethylene, expanded polytetrafluoroethylene, polytetrafluoroethylene/polyethylene copolymer, fluorinated ethylene propylene, polyvinylidene, hexafluroropropylene corresponding copolymers and blends; elastomers including polyurethane, polysiloxane, polyisoprene, silicone, styrene butadiene, natural

**Application No.:** 10/664,697 **Office Action Dated:** July 27, 2006

rubber, latex rubber, and corresponding copolymers and blends; engineering thermoplastics including polyethyleneterephthalate, polycarbonate, polyamide, polyaramid, polyaryl ether ketone, polyacetal, polyphenylene oxide, polysulfone, polyethersulfone, regenerated cellulose, polyamino acids, polyarylsulfone, polyphenylene sulfide, PBT, poly(glycolide), HEMA and the corresponding copolymers and blends; and

metallic materials selected from stainless steel, cobalt-chromium-molybdenum alloy, pure titanium, and titanium alloys.

- 27. (Original) The implant of Claim 26 wherein: the peptide MAP is selected from a MAP 4 or MAP 8.
- 28. (Original) The implant of Claim 27 wherein:

  R<sub>1</sub> to R<sub>8</sub> when present are selected from GTPGPQGIAGQRGVV (SEQ ID NO: 1) or
  RGD (SEQ ID NO: 2) and Z<sub>1</sub> to Z<sub>7</sub> are lysine and X<sub>1</sub> and X<sub>2</sub> are selected from β-ala-COOH,
  β-ala-CONH<sub>2</sub>, lys, or lys (NH<sub>2</sub>).
- 29. (Original) The implant of Claim 28 wherein S is selected from e-PTFE, PTFE, polysulfone, polyurethane, silicone, titanium or titanium alloy.